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10/580,446	05/23/2006	Yvonne Armitage	BT/3-22350/A/PCT	4199

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	PAPER NUMBER
1657	

NOTIFICATION DATE	DELIVERY MODE
03/31/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/580,446	ARMITAGE ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/08/2010 and 24 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 5-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5-9 and 11* is/are rejected.

7)☒ Claim(s) *10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1 and 5-11 as amended (1/08/2010) are pending and under examination.

Deposit

Deposit requirement for the strain *Rhodococcus rhodochrous* NCIMB 41164 has been met in papers filed 9/04/2008.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, 7, 8, 9 and 11 as amended remain/are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,705,382 (Endo et al).

Claims are directed to a method of producing an amide from the corresponding nitrile wherein the method comprises steps i) providing a microorganism capable of producing a nitrile hydratase biocatalyst, ii) culturing the microorganism in a growth medium, iii) storing the microorganism as "non-actively growing culture" in a storage medium comprising water and the growth medium, iv) contacting the nitrile with the microorganism in the storage medium without recovery the microorganisms using filtration, thereby converting the nitrile to the amide. Some claims are further drawn to producing amide such as ethylenically unsaturated amide or acrylamide. Some claims are further drawn to the use of storage temperature being above the freezing point of the storage medium for at least 2 days. Some claims are further drawn to the

use of microorganism belonging to the genus of *Rhodococcus* or to the species of *Rhodococcus rhodochrous*.

US 5,705,382 (Endo et al) discloses a method of producing an amide from the corresponding nitrile (entire document) wherein the method comprises steps providing a microorganism belonging to the species of *Rhodococcus rhodochrous* that is capable of producing a nitrile hydratase biocatalyst, step of culturing the microorganism in a growth medium with urea (col.7, lines 59-62); step of storing the microorganism at temperature above freezing point or at the very least at room temperature for 100 days (col. 8, line 14) and contacting the nitrile with the microorganism in an aqueous medium, thereby, converting the nitrile to the amide (col. 8, lines 18-30). The claimed "storing" step and/or manipulation with "storage medium" are drawn to intended effect of decreasing cell growth and metabolism during storage but are not limited by any special culture maintenance conditions except the use of components of a generic growth medium. It is well known that after initial exponential growth phase the rate of cell growth is decreased and the cell culture becomes "non-actively growing culture" during stationary phase. The claimed step of "converting the nitrile to the amide" is conducted in the presence of generic components of "storage" medium and, thus, recitation about exclusion/avoiding separation of cells from the "storage medium" does not explicitly pointed out what storage medium components would be retained during the step of converting as intended. US 5,705,382 (Endo et al) teaches the use of the same "storage" buffer in the step of "converting the nitrile to the amide". Thus, the step of "converting the nitrile to the amide" in the cited method cannot be reasonably distinguished from the claimed invention. Therefore, the cited method of US 5,705,382 (Endo et al) is still considered to anticipate the claimed invention.

Claims 1, 5-9 and 11 as amended are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,089,411 (Yamada et al).

Claims are directed to a method of producing an amide from the corresponding nitrile wherein the method comprises steps i) providing a microorganism capable of producing a nitrile hydratase biocatalyst, ii) culturing the microorganism in a growth medium, iii) storing the microorganism as "non-actively growing culture" in a storage medium comprising water and the growth medium, iv) contacting the nitrile with the microorganism in the storage medium without recovery the microorganisms using centrifugation or filtration, thereby converting the nitrile to the amide. Some claims are further drawn to producing amide such as ethylenically unsaturated amide or acrylamide. Some claims are further drawn to the use of storage temperature being above the freezing point of the storage medium for at least 2 days. Some claims are further drawn to the use of microorganism belonging to the genus of *Rhodococcus* or to the species of *Rhodococcus rhodochrous*.

US 5,089,411 (Yamada et al) discloses a method of producing an amide from the corresponding nitrile (entire document) wherein the method comprises steps providing a microorganism belonging to the species of *Rhodococcus rhodochrous* that is capable of producing a nitrile hydratase biocatalyst (col. 4, lines 65-69), step of culturing and/or storing the microorganism in a growth medium with urea at temperature above freezing point for at least 2 days or 120 hours (col. 5, lines 3-10) and contacting the nitrile with the microorganism in an aqueous medium, thereby, converting the nitrile to the amide (col. 6, lines 1-15; table 1 at col.7). The claimed "storing" step recites an intended effect of decreasing cell growth and metabolism but it is not limited by any special culture maintenance conditions except the use of components

of the same growth medium. It is well known that after initial exponential growth phase the rate of cell growth is decreased and the cell culture becomes "non-actively growing culture" during stationary phase. The claimed step of "converting the nitrile to the amide" is conducted in the presence of generic components of "storage" medium and, thus, recitation about exclusion/avoiding separation of cells from the "storage medium" does not explicitly pointed out what storage medium components would be retained during the step of converting as intended. Besides, US 5,089,411 (Yamada et al) solely recites that cells were isolated from a culture fluid (col. 6, lines 5) but not from any and all components of growth or storage media. Thus, the step of "converting the nitrile to the amide" in the cited method cannot be reasonably distinguished from the claimed invention. Therefore, the cited method of by US 5,089,411 (Yamada et al) is considered to anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5-9 and 11 as amended remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,705,382 (Endo et al), US 5,089,411 (Yamada et al), Nagasawa et al (IDS reference. Pure and Appl. Chem. 1996, Vol. 67, No. 7, pages 1241-1256) and US 6,395,467 (Fahy et al).

Claims are directed to a method of producing an amide from the corresponding nitrile wherein the method comprises steps i) providing a microorganism capable of producing a nitrile hydratase biocatalyst, ii) culturing the microorganism in a growth medium, iii) storing the microorganism as "non-actively growing culture" in a storage medium comprising water and the growth medium, iv) contacting the nitrile with the microorganism in the storage medium without recovery the microorganisms, thereby converting the nitrile to the amide. Some claims are further drawn to producing amide such as such as ethylenically unsaturated amide or acrylamide. Some claims are further drawn to the use of growth and storage media that comprise urea. Some claims are further drawn to the use of storage temperature being above the freezing point of the storage medium for at least 2 days. Some claims are further drawn to the use of microorganism belonging to the genus of *Rhodococcus* or to the species of *Rhodococcus rhodochrous*.

The cited patents US 5,705,382 (Endo et al) and US 5,089,411 (Yamada et al) are relied upon as explained above for the disclosure of a method for producing amides from the corresponding nitriles wherein the method comprises steps culturing or maintaining microorganisms belonging to the genus of *Rhodococcus* including representatives of the species of *Rhodococcus rhodochrous* in an aqueous medium comprising urea and converting nitriles to amides by using enzymatic activity of the microbial cells after prolonged storage or maintenance at temperature above freezing point. US 5,705,382 also discloses strain *Rhodococcus rhodochrous* such as strain J-1, for example: see US 5,705,382 col. 7, line 59, that is capable for producing both acrylamide (col. 8, line 27) and methacrylamide (see Nagasawa et al. at page 1248, lines 8-15) and which enzymatic activity is induced by the presence of urea.

Although in the particular example US 5,705,382 describes that *Rhodococcus rhodochrous* strain J-1 is immobilized as intended for preservation before production of amides, the cited patent US 5,705,382 clearly teaches that microbial cells having nitrile hydratase including representatives of the genus *Rhodococcus* activity can be stored either as free cell suspensions or as immobilized cells (col. 1, lines 54-65) in the method for producing amide (examples 4 and 7).

Both cited patents US 5,705,382 and US 5,089,411 (Yamada et al) clearly also teaches incorporation of urea in the culture medium for *Rhodococcus rhodochrous*. Further, US 5,089,411 (Yamada et al) explicitly teaches that incorporation of urea and its derivates increases enzymatic activity of *Rhodococcus rhodochrous* (entire document including abstract and col. 4, lines 10-35) without relative increase in cell concentration (table 1).

In addition, US 6,395,467 (Fahy et al) is relied upon to demonstrate that urea is a known ingredient of generic preservation solution intended fro storing biological materials, for example: see abstract.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use urea in the culture and/or storage media of *Rhodococcus rhodochrous* having nitrile hydratase activity with a reasonable expectation of success in converting nitriles to corresponding amides because the prior art teaches that incorporation of urea and its derivates increases enzymatic activity of *Rhodococcus rhodochrous*. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicant's arguments filed 9/24/2009 have been fully considered but they are not persuasive.

With regard to the claim rejection under 35 U.S.C. 102(b) as being anticipated by US 5,705,382 (Endo et al) applicants' main argument is that the cited method encompasses collecting cells by centrifugation after culturing step to remove growth medium (response page 4-5). This argument is not found persuasive for the very least reason that claims recite in alternative the exclusion of either centrifugation or filtration. Thus, even US 5,705,382 (Endo et al) recites centrifugation, it does not recite the use of "filtration". Further, most importantly, claimed method recites generic growth and storage media and it does not point out what "growth" and/or "storage" related ingredients would remain during converting step. The claimed step of "converting the nitrile to the amide" is conducted in the presence of generic components of "storage" medium and, thus, recitation about exclusion/avoiding separation of cells from the "storage medium" does not explicitly pointed out what storage medium components would be retained during the step of converting as intended. US 5,705,382 (Endo et al) teaches the use of the same "storage" buffer in the step of "converting the nitrile to the amide". Thus, the step of "converting the nitrile to the amide" in the cited method cannot be reasonably distinguished from the claimed invention.

With regard to the claim rejection under 35 U.S.C. 102(b) as being anticipated by US 5,089,411 (Yamada et al) applicants' main argument is that the cited method encompasses isolation of cells from culture fluid. Yet, the cited method recites exclusion of centrifugation or filtration. Further, most importantly, claimed method recites generic growth and storage media and it does not point out what "growth" and/or "storage" related ingredients would remain during converting step. Thus, the step of "converting the nitrile to the amide" in the cited method cannot be reasonably distinguished from the claimed invention.

With regard to the claim rejection under 35 U.S.C. 103 applicants' argument that the cited patents teach removal of growth medium components by centrifugation and washing before storing cells. This argument does not appear to have persuasive grounds because it is very well known that microbial cells could be stored at low temperature in the same medium in which they were grown. The claimed invention is generic with regard to storage conditions (claim 1, for example). Although the claim 6 is directed to the use of urea, the use of urea in the specially designed storage media have been known in the prior art. Thus, the teaching of the cited references taken as a whole cannot be distinguished from the invention as presently claimed.

Applicants also appear to argue that "it has surprisingly been found that during the storage period the activity of the biocatalyst comprising nitrile hydratase activity actually increases (page 9, lines 29-30) which is also shown in Example 1 of the present application". Upon review it is not found particularly persuasive. First, specification describes that the biocatalyst comprising nitrile hydratase activity provides for increase in enzyme activity when cells are stored at low temperature as compared to maintenance at room temperature (page 15).

However, the instant claims are not limited to the specific conditions that provide for unexpected effects, if any. Furthermore, the particular examples (page 14) describe that cells were actually separated by centrifugation from the components of "growth" and storage" media and, thus, the contents of specification and arguments based thereon are rather confusing as to the significance of the differences between prior art method and the claimed method.

With respect to the claim 10, drawn to the use of a specific novel strain NCIB 41164, it is noted that claim 10 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached at (571) 272-0925.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

March 25, 2010

/Vera Afremova/

Primary Examiner, Art Unit 1657